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TITLE: **The Use of Quantitative SPECT/CT Imaging to Assess Residual Limb Health**

PRINCIPAL INVESTIGATOR: **Christopher L. Dearth, PhD**

CONTRACTING ORGANIZATION: **The Henry M. Jackson Foundation for the
Advancement of Military Medicine, Inc.
Bethesda, MD 20817**

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14. ABSTRACT The objective of the proposed study is to translate SPECT/CT imaging to patients with lower extremity amputation and subsequently evaluate the utility of non-invasive imaging for evaluating the impact of next-generation socket technologies on the health of the residual limb. It is hypothesized that SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to assess changes in microvascular perfusion elicited by next-generation prosthetic socket technologies and that acute changes in microvascular perfusion will be predictive of long term residual limb health outcomes. While the project timeline is currently slightly behind / delayed from our initial projection, the study team has taken significant actions towards remedying these issues and is very confident that we can get the project back on track in short order and drive towards a successful end point – which will greatly benefit our patients.					
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Table of Contents

	<u>Page</u>
1. Introduction.....	4
2. Keywords.....	4
3. Accomplishments.....	5-6
4. Impact.....	7
5. Changes/Problems.....	7-8
6. Products.....	8-9
7. Participants & Other Collaborating Organizations.....	9
8. Special Reporting Requirements.....	10-11

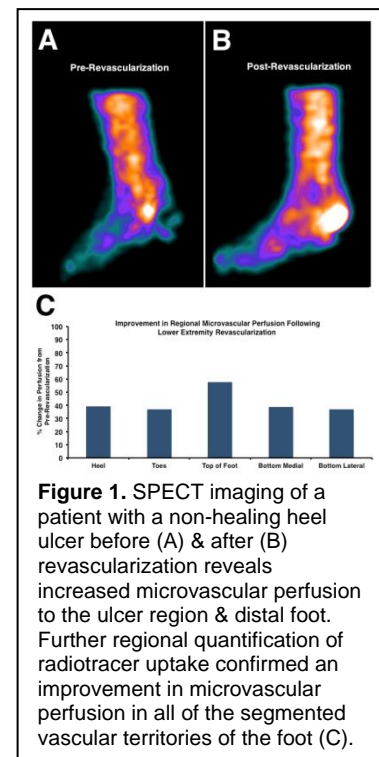
INTRODUCTION:

Prosthetic devices aim to restore the appearance and/or function of the affected extremity for patients with amputations. The socket is a critical feature of a prosthetic device as it acts as the interface between the prosthesis and residual limb. Numerous residual limb health issues have been associated with traditional socket technologies. Accordingly, the DoD has invested significant effort and funding in recent years to facilitate the development of improved socket technology to aid in the maintenance of tissue health in the residual limb. While these efforts are beginning to yield exciting next-generation socket technologies (e.g., ‘smart’ sockets), limited technologies are available to assess the impact of these sockets on the underlying physiological response in the residual limb.

The health of residual limb tissue in persons with lower-limb amputation is of critical importance. Breakdown of tissue viability of the residual limb can negatively impact the progress of the patient’s rehabilitation and/or lead to prosthesis abandonment, thus reducing their mobility, function, and overall quality of life. To date, the ability to accurately assess tissue viability within the residual limb of individuals with amputations while the socket is on has been challenging. Therefore, a non-invasive, sensitive, and quantitative imaging modality that could provide an objective assessment of the overall health of the residual limb would advance the standard of care for affected patients, as well as improve selection of the most effective socket technologies at promoting overall limb health.

In accordance with the intent of the FY14 OPOP award mechanism, the goal of the current research study is to provide outcomes data to inform and improve the care of military service members with lower extremity amputation(s). This will be accomplished by utilizing a validated SPECT/CT imaging technique to assess which prosthetic socket technologies will generate the best patient outcomes (i.e., residual limb health) for service members with limb loss. Successful completion of this study would significantly improve our understanding and advance the implementation of the prosthetic socket devices most effective at promoting the overall health of the residual limb, thereby greatly benefiting patient care.

KEYWORDS: Prosthetics, residual limb health, imaging, extremity trauma, amputation



ACCOMPLISHMENTS:

What were the major goals of the project?

The objective of the proposed study is to translate SPECT/CT imaging to patients with lower extremity amputation and subsequently evaluate the utility of non-invasive imaging for evaluating the impact of next-generation socket technologies on the health of the residual limb. It is hypothesized that SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to assess changes in microvascular perfusion elicited by next-generation prosthetic socket technologies and that acute changes in microvascular perfusion will be predictive of long term residual limb health outcomes.

<i>Specific Aim 1 - To quantify basal microvascular perfusion and perfusion reserve of the residual limb in patients with lower extremity amputation using SPECT/CT imaging.</i>	Target Dates (months)	Percentage Completion
Major Task 1: To evaluate SPECT/CT imaging as a means to assess limb health in patients with amputation.		
Subtask 1.1 – WRNMMC IRB Approval	1-6	75%
Subtask 1.2 – Yale University IRB Approval	1-6	100%
Subtask 1.3 – HRPO Approval	1-6	0%
Subtask 1.4 – Human subject testing of SPECT/CT imaging	6-18	0%
Subtask 1.5 – Image analysis and quantification	6-18	0%
Subtask 1.6 – Dissemination of results describing SPECT/CT imaging in an amputee population	18-20	0%
<i>Specific Aim 2 - To evaluate the efficacy of next-generation (e.g., breathable socket) prosthetic socket technologies at promoting tissue health of the residual limb of patients with lower extremity amputation using SPECT/CT imaging.</i>	Target Dates (months)	Percentage Completion
Major Task 2: To use SPECT/CT imaging to evaluate new socket technologies on the long term limb health in patients with amputation.		
Subtask 2.1 – Long term follow up SPECT/CT imaging of 40 subjects	12-22	0%
Subtask 1.5 – Image analysis and quantification of long term follow up imaging	12-22	0%
Subtask 1.6 – Dissemination of results describing use SPECT/CT imaging to evaluate new socket technologies on the long term limb health in patients with amputation.	22-24	0%

What was accomplished under these goals?

During the current reporting period, considerable effort has been devoted towards completion the current project, specifically towards the establishment of the project specific infrastructure:

- Study kickoff meeting completed at WRNMMC (09/10/2015)
- Initiated and conducted bi-weekly teleconferences

- Devoted significant efforts towards getting the subcontract set up with Yale University (via HJF)
- A CRADA b/w HJF, WRNMMC, and Yale University is being developed
- Conducted a two day project team meeting / site visit (April 2016) which resulted in significant work products / project progress
- Creation of a draft clinical research protocol and associated regulatory documents by the PI and Co-PI
- The position description (PD) for Post-Doctoral fellow (which will devote 100% effort toward this project) was developed
- Posted / advertised the PD for open position
- The project team has reviewed ~25 applications for the research staff position and is in the process of interviewing numerous candidates

What opportunities for training and professional development has the project provided?

Nothing to Report.

Training and professional development are not a focus of this work.

How were the results disseminated to communities of interest?

Nothing to Report.

No results generated as yet.

Dissemination is planned for year 2 of the project.

What do you plan to do during the next reporting period to accomplish the goals?

Our main goal for the beginning of the next reporting period is to achieve full regulatory approval (IRB & HRPO) for the clinical protocol such that we can begin subject enrollment.

Another goal is to hire the research support personnel for this project – as this individual will be assisting with recruitment, data collection & analysis, etc... we have been mindful to try to synchronize the on-board and regulatory approval dates as closely as possible (i.e., we do not to hire this person ‘too soon’ [i.e., well before the protocol is approved] such that we do not ‘waste’ money by having the individual spending down money with nothing to do)

IMPACT:

We expect that this project will significantly improve our understanding and advance the implementation of the prosthetic socket devices most effective at promoting the overall health of the residual limb, thereby greatly benefiting patient care.

What was the impact on the development of the principal discipline(s) of the project?

Nothing to Report.

What was the impact on other disciplines?

Nothing to Report.

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report.

CHANGES/PROBLEMS:**Changes in approach and reasons for change**

Nothing to Report.

Actual or anticipated problems or delays and actions or plans to resolve them

The project timeline is currently slightly behind / delayed from our initial projection. This delay was due, in part, to the significant delays that were encountered with setting up the sub-award with Yale, and significant delays incurred due to the implementation of the new online DoD IRB system.

The study team has taken significant actions towards remedying these issues, including working closely the appropriate PoCs at HJF and Yale to help shepherd the sub-award forward without

any further delays, coordinated with the new WRNMMC IRB SRC Chair regarding moving this process forward, and spent a significant amount of time learning and troubleshooting the new IRB system such that our team is now able to successfully create and submit a new protocol within the system. Taken together, the study team is very confident that we can get the project back on track in short order and drive towards a successful end point – which will greatly benefit our patients.

Changes that had a significant impact on expenditures

Nothing to Report.

Expenditures are significantly less than originally budgeted at this point in the study.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to Report.

PRODUCTS:

Journal publications.

The study team was invited to contribute manuscripts to a special issue of *Advances in Wound Care* which is dedicated to “Amputee Care and Rehabilitation”. The focus of these knowledge products was that of this funded project – i.e., highlighting the importance of advanced imaging modalities in evaluating residual limb health of service members and veterans with limb loss.

- **Mitchel R. Stacy** and **Christopher L. Dearth**. “*Multimodality imaging approaches for evaluating traumatic extremity injuries: implications for military medicine*”. Advances in Wound Care. 2016 (In Press)
- Courtney Butowicz, **Christopher L. Dearth**, Brad D. Hendershot. “*Impact of traumatic lower extremity injuries beyond acute care: Movement-based considerations for resultant long-term secondary health conditions*”. Advances in Wound Care. 2016 (In Press)

Books or other non-periodical, one-time publications.

Nothing to Report.

Other publications, conference papers, and presentations.

Nothing to Report.

Website(s) or other Internet site(s)

Nothing to Report.

Technologies or techniques

Nothing to Report.

Inventions, patent applications, and/or licenses

Nothing to Report.

Other Products

Nothing to Report.

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Christopher L. Dearth, PhD
Project Role: Principle Investigator

Name: Mitchel R. Stacy, PhD
Project Role: Co-Principle Investigator

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to Report. No changes have been made to efforts on this project.

What other organizations were involved as partners?

No new organizations were involved as partners (besides the Yale University School of Medicine as originally proposed).

SPECIAL REPORTING REQUIREMENTS

QUAD CHART:

(See next page)

The Use of Quantitative SPECT/CT Imaging to Assess Residual Limb Health



Orthotics and Prosthetics Outcomes Research Award - W81XWH-15-1-0669

PI: Christopher L. Dearth, PhD **Org:** Walter Reed National Military Medical Center **Award Amount:** \$484,210

Objective: The objective of the proposed proof of concept, pilot clinical study is to translate ^{99m}Tc -tetrofosmin SPECT/CT imaging to patients with lower extremity amputation and subsequently evaluate its effectiveness as a means to evaluate the impact of next generation socket technologies on the health of the residual limb. This objective will be evaluated by the following specific aims:

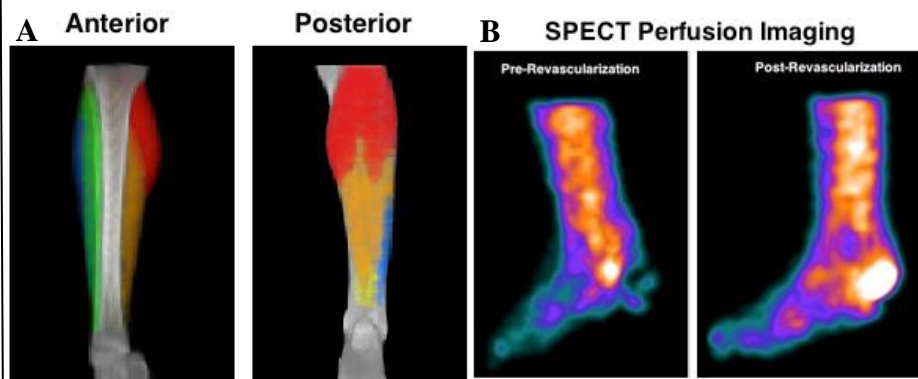
Specific Aim 1: To quantify basal microvascular perfusion and perfusion reserve of the residual limb in patients with lower extremity amputation using ^{99m}Tc -tetrofosmin SPECT/CT imaging.

Hypothesis: It is hypothesized that evaluation of microvascular perfusion via ^{99m}Tc -tetrofosmin SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to use during the assessment of residual limb tissue health beyond traditional limb health outcome measures.

Specific Aim 2: To evaluate the efficacy of current (e.g., VASS) and next-generation (e.g., breathable socket) prosthetic socket technologies at promoting tissue health of the residual limb of patients with lower extremity amputation using ^{99m}Tc -tetrofosmin SPECT/CT imaging.

Sub Aim 2.1 - To determine if acute changes in microvascular perfusion are predictive of long term residual limb health outcomes.

Hypothesis: It is hypothesized that ^{99m}Tc -tetrofosmin SPECT/CT imaging will provide a highly sensitive, non-invasive tool for clinicians to assess changes in microvascular perfusion elicited by next-generation prosthetic socket technologies and these acute changes in microvascular perfusion will be predictive of long term residual limb health outcomes.



A) Anterior & posterior views of 3-D calf muscle regions segmented from a CT attenuation scan. Gastrocnemius (red), soleus (orange), tibialis anterior (green), tibialis posterior (yellow), and fibularis longus (blue) muscles are displayed and overlaid on a bone only CT image. **B)** ^{99m}Tc -tetrofosmin SPECT perfusion imaging in a patient with a non-healing heel ulcer prior to and following lower extremity revascularization demonstrates increased radiotracer uptake in the site of the heel ulcer and distal foot following treatment.

Timeline and Cost

Activities	Calendar Year (Funding Year)	2015	2016 (1)	2017 (2)
IRB creation / submission / approval				
Begin subject recruitment / enrollment				
Specific Aim #1				
Specific Aim #2				
Study Completion / Data Dissemination				
Budget (\$K)			\$244	\$240

Goals / Milestones

CY15 Goals – Initiation / IRB / Personnel

- ☒ Study kickoff meeting
- ☒ Clinical research protocol generation
- ☒ Generation of position description for research personnel

CY16 Goal – Study Initiation / Data Collection

- ☒ WRNMMC IRB SRC submission
- ☐ Full WRNMMC IRB Approval
- ☐ Begin subject recruitment / enrollment
- ☐ Begin data collection for SA 1 & 2

CY17 Goal – Study Completion

- ☐ Complete data collection for SA 1 & 2
- ☐ Manuscript(s) submission / publication
- ☐ Conference abstract submission / presentation